

# Fiber Density Mapping in Patients with Gliomas: Histopathologic evaluation of a novel approach for post-processing of DTI data

A. Stadlbauer<sup>1,2</sup>, M. Buchfelder<sup>2</sup>, and O. Ganslandt<sup>2</sup>

<sup>1</sup>MR Physics Group, Department of Radiology, Landeskrankenhaus St. Poelten, St. Poelten, Austria, <sup>2</sup>Department of Neurosurgery, University of Erlangen-Nuremberg, Erlangen, Germany

**Introduction:** Knowledge about the involvement of white matter structures in the border zone of gliomas is essential for the planning of neurosurgical therapy strategies. Diffuse infiltration of tumor cells into normal brain parenchyma and the invasive growth patterns of gliomas pose a problem in imaging strategies. MR diffusion tensor imaging (DTI) allows for studying the white matter fibers structures. DTI data are usually evaluated by calculating parametric maps (fractional anisotropy, FA, or mean diffusivity, MD) or by fiber tracking which enables reconstruction of white matter pathways in three dimensions. Fiber density mapping (FDM) is a new approach for post-processing of DTI data. Fiber density (FD) is as an indicator of the density of white matter fibers within the bundle passing through a voxel or a region of interest. FDM is a 2-step post-processing strategy: first, the reconstruction of all fiber paths for the whole brain from the volumetric DTI data using a tracking algorithm and tracking thresholds (e.g. for FA, track turning angle, etc.); and second, the depiction of the individual FD values for each voxel as parametric maps of the whole brain. The purpose of this paper was the histopathological evaluation of FDM in glioma patients to assess the extent of destruction of white matter structures due to the pathologic processes in the center, the transition zone and the border zone of the tumor.

**Methods:** We correlated FDM data and histopathological findings from MRI-guided stereotactic biopsies of 20 patients (18–53 y) with a supratentorial glioma WHO grade II (seven patients) or III (13 patients). DTI data were obtained using a diffusion-weighted EPI sequence (TR/TE = 9200/86 ms) with six diffusion directions ( $b = 1000 \text{ s/mm}^2$ ), an isotropic voxel size of  $1.9 \text{ mm}^3$ , 60 slices with no gap and 5 averages. The volume of interest (VOI) was chosen to cover the whole brain. Fiber tracking using DTI-Studio and the Fiber Assignment by Continuous Tracking (FACT) method was performed to calculate FD values for all voxels within the VOI. The tracking procedure were stopped for a FA threshold = 0.1 and/or a tract turning-angle  $>70^\circ$ . Coregistration of FDM data with a 3D MPRAGE data set and a T2-weighted TSE data set, which were used for stereotactic brain biopsies, allowed correlation of FD values with histopathological findings expressed as % tumor infiltration and tumor cell number (tumor CN) (**Fig.1**). Additionally, FD values for fiber structures in contralateral normal white matter structures (cNWM) were determined for normalization of pathologic FD changes.

**Results:** The histopathologic findings of 78 MR image-guided stereotactic biopsies from all 20 patients were correlated with the corresponding FD values at the biopsy locus. For FD we found a strong negative logarithmic correlation with both, the % tumor infiltration ( $R = -0.909$ ,  $p < 0.001$ ,  $FD = -10.65 \cdot \ln[\%TI] + 46.95$ , **Fig.2A**) and the number of tumor cells ( $R = -0.810$ ,  $p < 0.001$ ,  $FD = -7.59 \cdot \ln[\text{tumorCN}] + 40.54$ , **Fig.2B**). Complete destruction of white matter structures, i.e.  $FD = 0$ , were found for a tumor cell infiltration  $\geq 60\%$  and a tumor CN  $\geq 150$ . Fiber structures in the transition zone and the border zone of the tumors (i.e. % tumor infiltration  $< 60\%$  and tumor CN  $< 150$ ) showed a range of mean FD values of 0 – 41. Fiber structures in cNWM showed a range of mean FD values of 18 – 42 (mean value  $\pm$  SD,  $31 \pm 8$ ). A FD value of 18 (i.e. the lower limit for the FD values in cNWM) is related to a tumor infiltration of approx. 16% as calculated from our histopathology-versus-fiber density model.

**Discussion:** In this study we presented a novel approach for post-processing of DTI data. We correlated FDM data with histopathological findings from MRI-guided stereotactic biopsies and found a logarithmic correlation with both, % tumor cell infiltration and tumor CN. For a tumor infiltration of  $>60\%$  (150 tumor cells) no fiber structures are remaining. In regions with a tumor infiltration of  $<60\%$  and  $>16\%$  fiber structures still exists, but they are certainly functionally not important. However, in tumor regions with  $<16\%$  tumor cells functional important fiber structures may still exists. Our model of histopathology-versus-fiber density may be helpful for preoperative planning of neurosurgical treatment to prevent post-therapeutic neurologic deficits.

